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Sex-differences in adiponectin levels and body fat distribution: longitudinal observations in Afro-Jamaicans

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Summary

We longitudinally explored the relationship of body size and adiponectin levels in 393 community-dwelling Afro-Jamaicans. Adiponectin levels were greater in women, increased with age and declined with abdominal adiposity. Multivariate regression analyses suggest that subcutaneous fat in women may contribute significantly to the variance in their adiponectin levels.

Keywords

adiponectin; adiposity; waist; hip; sex; Jamaica

Introduction

Adiponectin, an adipocytokine, has effects on glucose homeostasis and regulation of energy metabolism [1]. In many ethnic groups, circulating adiponectin levels are lower in patients with type 2 diabetes, obesity, and cardiovascular disease [2]. Similarly, we previously showed that adiponectin is an independent predictor of glucose intolerance in Afro-Jamaicans [3]. In this study, we evaluated the clinical and anthropometric characteristics that determine adiponectin levels in non-diabetic, community-dwelling Afro-Jamaicans.

Materials and Methods

The International Collaborative Study of Hypertension in Blacks (ICSHIB) study was an observational study that examined the prevalence of hypertension and other non-communicable chronic diseases in the African Diaspora [4]. At the site in Jamaica, 2635 urban persons, ages 25-74 years, were recruited between 1993 and 1995 as previously described [3,5]. Anthropometry (weight, height, hip and waist circumferences) was measured using the ICSHIB standardized protocol [4] and a 75-g oral glucose tolerance test was performed. The prevalence of diabetes was 13.4% [5]. In 1998-2000 (mean interval: 4.1

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± 0.9 yrs), 1136 persons were re-measured. For adiponectin measurement [3], we selected participants who were normoglycaemic at baseline (i.e. fasting plasma glucose ≤ 6.0 mmol/l and 2-hour glucose < 7.8 mmol/l) and who had adequate serum for hormonal assays (n=393). The protocol was approved by the Faculty of Medical Sciences/University Hospital of the West Indies Ethics Committee.

Serum adiponectin was measured by ELISA (Linco Research, MI, USA; sensitivity of 0.78 ng/ml). The intra-assay and inter-assay coefficients of variations of the assay were $\leq 8\%$. Serum insulin measured by immunometric assay (Immulite, Diagnostic Products Corporation, CA, USA). Insulin resistance (HOMA-IR) was calculated using the HOMA2 Calculator v2.2 (www.dtu.ox.ac.uk/homa). HOMA-IR and adiponectin data were log transformed and Student's *t*-test was used to compare differences between means. Pearson correlation coefficients were used to explore the relationships of adiponectin at follow-up and baseline variables. Multiple linear regression models were used to explore the associations of anthropometric variables with adiponectin at follow-up.

Results

At baseline and 4.1 years later, women were younger, heavier, more insulin resistant, and had higher hip circumferences, 2-hour glucose and adiponectin levels (*P*-values < 0.05 ; Table 1). Weight, BMI, waist, WHR, fasting glucose, 2-hour glucose, HOMA-IR, and adiponectin changed significantly (*P*-values < 0.01) over 4.1 years in both sexes. These changes were not different by sex.

In univariate analyses, adiponectin had significant inverse correlations with baseline weight, waist, hip, BMI, WHR, HOMA-IR (*P*-values < 0.001), but not for 2-hour glucose at baseline and follow-up (data not shown). In separate age and sex-adjusted multivariate models, baseline waist and baseline BMI each predicted adiponectin at follow-up (Table 2). With further adjustment for hip circumference, female sex was no longer an independent predictor. In a model with waist and hip entered separately, waist remained inversely correlated ($\beta = -0.72$; $P \leq 0.001$), but hip was positively correlated ($\beta = 0.54$; $P \leq 0.001$). Models with baseline adiponectin, baseline weight, BMI, change in waist, or baseline HOMA-IR in place of waist circumference yielded similar results (data not shown). Anthropometric variables were not significantly associated with change in adiponectin (*P*-values > 0.1 ; data not shown).

Discussion

Serum concentrations of adiponectin increase with age, are greater in women, and decline with abdominal adiposity in this longitudinal cohort of community-dwelling Afro-Jamaicans. It is intriguing that adiponectin increases with age, despite the fact that the subjects became more heavy and insulin resistant. This effect has been seen by other investigators [6] and while declining renal clearance may be a factor [7], the true cause is unclear.

Although women were more obese and insulin resistant, they had higher levels of adiponectin. This sexual dimorphism may be due to a selective increase in high molecular weight oligomers in women [8]. Also, androgens inhibit the production of adiponectin in animal models [9] and tissue culture of adipocytes [10]. Men have greater visceral fat mass than women, even after adjusting for BMI [11] and women have more subcutaneous fat. Thus, a complementary theory is that subcutaneous adipocytes may play a role in adiponectin levels. Some authors contend that subcutaneous fat does not produce significant amounts of adiponectin [2]. However, our data suggest that fat topography may be a factor,

i.e. the greater amounts of subcutaneous fat in women (as represented by hip circumference and waist-hip ratio) contribute significantly to the variance in their adiponectin levels. In support of this concept, subcutaneous fat in the lower limbs of Dutch men is positively associated with adiponectin levels [12]. In addition, adiponectin was positively associated with subcutaneous fat but inversely related to visceral fat in Japanese men [13].

Conceivably, as many individuals gain weight during ageing, subcutaneous adipocytes accumulate intracellular triacylglycerols and then secrete more adiponectin. However, some predisposed persons (e.g. men and ethnic groups such as Southeast Asians) may have limiting depots of subcutaneous fat or may be metabolically constrained from increasing their triacylglycerol depots in subcutaneous adipocytes. Therefore, positive caloric balance in these individuals would result in more overflow into the visceral compartment – the so-called adipose tissue overflow hypothesis [14]. Hypertrophy of visceral adipocytes leads to secretion of inflammatory cytokines (e.g. IL-6, TNF- α) which by autocrine, paracrine and endocrine action would decrease adiponectin secretion from visceral adipocytes [2], as well as decrease whole body insulin sensitivity. If this is true, an expanded visceral fat compartment would lead to the partially independent outcomes of relative hypoadiponectinaemia and insulin resistance. Women have more adipocytes in the subcutaneous compartment than men [15], and their adipocytes are larger, with a greater capacity for fat storage. Consequently, weight gain in men may disproportionately increase the visceral compartment and produce relative hypoadiponectinaemia.

In summary, adiponectin levels increase with age, are greater in women, and decline with abdominal adiposity. The greater amounts of subcutaneous fat in women may contribute significantly to the variance in their adiponectin levels.

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References

1. Kadowaki T, Yamauchi T. Adiponectin and adiponectin receptors. *Endocr Rev* 2005;26:439–45. [PubMed: 15897298]
2. Swarbrick MM, Havel PJ. Physiological, pharmacological, and nutritional regulation of circulating adiponectin concentrations in humans. *Metab Syndr Relat Disord* 2008;6:87–102. [PubMed: 18510434]
3. Bennett NR, Boyne MS, Cooper RS, Royal-Thomas TY, Bennett FI, Luke A, et al. Impact of adiponectin and ghrelin on incident glucose intolerance and on weight change. *Clin Endocrinol (Oxf)* 2009;70:408–414. [PubMed: 18624998]
4. Cooper R, Rotimi C, Ataman S, McGee D, Osotimehin B, Kadiri S, et al. The prevalence of hypertension in seven populations of west African origin. *Am J Public Health* 1997;87:160–168. [PubMed: 9103091]
5. Wilks R, Rotimi C, Bennett F, McFarlane-Anderson N, Kaufman JS, Anderson SG, et al. Diabetes in the Caribbean: results of a population survey from Spanish Town, Jamaica. *Diabet Med* 1999;16:875–883. [PubMed: 10547216]
6. Cnop M, Havel PJ, Utzschneider KM, Carr DB, Sinha MK, Boyko EJ, et al. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. *Diabetologia* 2003;46:459–469. [PubMed: 12687327]
7. Isobe T, Saitoh S, Takagi S, Takeuchi H, Chiba Y, Katoh N, et al. Influence of gender, age and renal function on plasma adiponectin level: the Tanno and Sobetsu study. *Eur J Endocrinol* 2005;153:91–98. [PubMed: 15994750]

8. Pajvani UB, Du X, Combs TP, Berg AH, Rajala MW, Schulthess T, et al. Structure-function studies of the adipocyte-secreted hormone Acrp30/adiponectin. Implications for metabolic regulation and bioactivity. *J Biol Chem* 2003;278:9073–9085. [PubMed: 12496257]
9. Bottner A, Kratzsch J, Muller G, Kapellen TM, Bluher S, Keller E, et al. Gender differences of adiponectin levels develop during the progression of puberty and are related to serum androgen levels. *J Clin Endocrinol Metab* 2004;89:4053–4061. [PubMed: 15292348]
10. Xu A, Chan KW, Hoo RL, Wang Y, Tan KC, Zhang J, et al. Testosterone selectively reduces the high molecular weight form of adiponectin by inhibiting its secretion from adipocytes. *The Journal of biological chemistry* 2005;280:18073–18080. [PubMed: 15760892]
11. Sumner AE, Farmer NM, Tulloch-Reid MK, Sebring NG, Yanovski JA, Reynolds JC, et al. Sex differences in visceral adipose tissue volume among African Americans. *Am J Clin Nutr* 2002;76:975–979. [PubMed: 12399268]
12. Frederiksen L, Nielsen TL, Wraae K, Hagen C, Frystyk J, Flyvbjerg A, et al. Subcutaneous rather than visceral adipose tissue is associated with adiponectin levels and insulin resistance in young men. *J Clin Endocrinol Metab* 2009;94:4010–4015. [PubMed: 19755479]
13. Nakamura Y, Sekikawa A, Kadowaki T, Kadota A, Kadowaki S, Maegawa H, et al. Visceral and subcutaneous adiposity and adiponectin in middle-aged Japanese men: the ERA JUMP study. *Obesity (Silver Spring)* 2009;17:1269–1273. [PubMed: 19584883]
14. Sniderman AD, Bhopal R, Prabhakaran D, Sarrafzadegan N, Tchernof A. Why might South Asians be so susceptible to central obesity and its atherogenic consequences? The adipose tissue overflow hypothesis. *Int J Epidemiol* 2007;36:220–225. [PubMed: 17510078]
15. Drolet R, Richard C, Sniderman AD, Mailloux J, Fortier M, Huot C, et al. Hypertrophy and hyperplasia of abdominal adipose tissues in women. *Int J Obes (Lond)* 2008;32:283–291. [PubMed: 17726433]

Table 1

Body composition and metabolic variables by sex at baseline and at follow-up in 393 community-dwelling Afro-Jamaicans (144 men and 249 women) over a mean period of 4.1 years
Data are means $\pm$ SD.

Variable	Baseline		Follow-up	
	Men	Women	Men	Women
Age (yrs)	49.2 $\pm$ 14.0 [*]	45.7 $\pm$ 13.1	53.2 $\pm$ 14.1 [*]	49.9 $\pm$ 13.2
Weight (kg)	71.4 $\pm$ 13.1 [*]	74.7 $\pm$ 17.1	73.7 $\pm$ 14.4 [*]	77.4 $\pm$ 17.5
Height (cm)	171.4 $\pm$ 5.8 [‡]	161.4 $\pm$ 6.5	171.5 $\pm$ 5.8 [‡]	161.3 $\pm$ 6.3
BMI (kg/m ²)	24.2 $\pm$ 4.2 [‡]	28.6 $\pm$ 6.4	25.0 $\pm$ 4.6 [‡]	29.7 $\pm$ 6.5
Hip (cm)	96.6 $\pm$ 8.0 [‡]	105.6 $\pm$ 12.5	98.1 $\pm$ 8.4 [‡]	107.7 $\pm$ 12.7
Waist (cm)	81.9 $\pm$ 11.5	84.3 $\pm$ 12.3	85.7 $\pm$ 12.9	88.3 $\pm$ 12.7
Waist to hip	0.85 $\pm$ 0.07 [‡]	0.80 $\pm$ 0.05	0.87 $\pm$ 0.07 [‡]	0.82 $\pm$ 0.06
2 hour glucose (mmol/L)	5.8 $\pm$ 1.8 [‡]	6.3 $\pm$ 1.6	7.3 $\pm$ 2.5 [*]	7.9 $\pm$ 2.7
Fasting glucose (mmol/L)	4.8 $\pm$ 0.7	4.8 $\pm$ 0.7	5.2 $\pm$ 0.9	5.1 $\pm$ 1.3
HOMA-IR	0.60 $\pm$ 0.41 [‡]	1.0 $\pm$ 0.76	0.69 $\pm$ 0.43 [‡]	1.08 $\pm$ 0.66
Adiponectin	7.97 $\pm$ 4.20 [‡]	9.39 $\pm$ 4.61	8.55 $\pm$ 4.18 [‡]	9.95 $\pm$ 4.38

* Notes: *P* value <0.05, significant difference between men and women;

[‡] *P* value <0.01, significant difference between men and women;

[‡] *P* value <0.001, significant difference between men and women.

Table 2

Separate multivariate models showing the effect of age, sex and anthropometry on the dependent variable, adiponectin ($\mu\text{g/ml}$) at follow-up 4.1 years later in 393 community-dwelling Afro-Jamaicans

Model	Coefficient (B $\pm$ SE)	Standardized coefficient (β)	P-value	Adjusted R ²
Age (yrs)	0.004 $\pm$ 0.001	0.31	<0.001	0.14
Female sex	0.112 $\pm$ 0.021	0.27	<0.001	
BMI (kg/m^2)	-0.006 $\pm$ 0.002	-0.018	0.001	
Age (yrs)	0.005 $\pm$ 0.001	0.34	<0.001	0.19
Female sex	0.098 $\pm$ 0.019	0.24	<0.001	
Waist (cm)	-0.005 $\pm$ 0.001	-0.28	<0.001	
Age (yrs)	0.004 $\pm$ 0.001	0.30	<0.001	0.13
Female sex	0.106 $\pm$ 0.021	0.26	<0.001	
Hip (cm)	-0.002 $\pm$ 0.001	-0.13	0.01	
Age (yrs)	0.006 $\pm$ 0.001	0.43	<0.001	0.25
Female sex	0.029 $\pm$ 0.019	0.07	0.13	
Waist-hip ratio	-1.270 $\pm$ 0.152	-0.47	<0.001	